

Application No.: 09/859,701 : Examiner: Davis, Deborah A.
Filed: May 16, 2001 : TC/A U: 1655
Applicant: Warner, Benjamin P. : Confirmation No.: 4132
Docket No.: 60184.24 : Customer No.: 27128
Title: METHOD FOR DETECTING BINDING EVENTS USING MICRO-X-
RAY FLUORESCENCE SPECTROMETRY

Via EFS-Web

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DECLARATION OF GEORGE J. HAVRILLA
PURSUANT TO 37 C.F.R. § 1.132

1. I am an inventor of the above-identified U.S. patent application.

2. I have been a Technical Staff Member with Los Alamos National Laboratory, based in Los Alamos, New Mexico, since 1993. My focus is on chemistry and engineering sciences and my primary area of research involves spectroscopic methods for materials characterization including elemental and molecular spectroscopic methods of analysis. My research further includes X-ray fluorescence; infrared and Raman spectroscopic methods; chemical imaging and chemometric-based data processing technology for both elemental and molecular identification of species; X-ray optics applications for the development of three-dimensional elemental mapping of materials; and laboratory-based X-ray absorption instrumentation. Immediately prior to my present employment, I was employed by BP Research and Environmental Science Center, based in Cleveland, Ohio from 1982-1992. While at BP Research and Environmental Science Center, I was a Senior Project Leader from 1990-1992, a

Project Leader from 1984-1990, and a Senior Research and Development Chemist from 1982-1984. While at BP Research and Environmental Science Center, my research included X-ray fluorescence; laser analysis; and particle technology.

3. I received a Ph.D. in Chemistry from West Virginia University in 1980. While at WVU, my research focused on analytical chemistry emphasizing laser-based trace element detection and atomic spectrometry. I received a M.S. in Chemistry from State University of New York at Stony Brook in 1976. While there, my research focused on physical organic chemistry involving spectroscopic study of molecular species. I received a B.S. in Chemistry from the University of Scranton in 1974.

4. I have won several awards for my work including two R&D 100 Awards from R&D Magazine in 2004 and 2005. I received the designation of Fellow from the International Centre for Diffraction Data in 2002. I also received Poster Awards at the Denver X-Ray Conference in 1997 and 2003 and from the Federation of Analytical Chemistry and Spectroscopy Societies in 2003. I also received a Team Distinguished Performance Award from Los Alamos National Laboratory in 2000.

5. Selected publications of mine include:

- (i) Integrating X-Ray Fluorescence and Infrared Imaging Microspectroscopies for Comprehensive Characterization of An Acetaminophen Model Pharmaceutical. B. Patterson and G. Havrilla; Applied Spectroscopy, 2006, 60(5), 471-478.
- (ii) Automated Printing Technology As A New Tool For Liquid Sample Preparation For Micro X-Ray Fluorescence (MXRF). T. Miller, E. Hastings, and G. Havrilla, X-ray Spectrometry, 2006, 35, 131-136.

- (iii) Three-Dimensional Elemental Imaging Using a Confocal X-ray Fluorescence Microscope. G. Havrilla and B. Patterson; American Laboratory, (2006) 38 (8), 15-22.
- (iv) Characterization of small particles by micro X-ray fluorescence. T. Miller, H. DeWitt, and G. Havrilla; Spectrochimica Acta Part B 2005 (60) 1458-1467.
- (v) High-throughput screening with micro-x-ray fluorescence. G. Havrilla and T. Miller; Virtual Journal of Biological Physics Research, June 1, 2005, Volume 9, Issue 11.
- (vi) Micro X-ray fluorescence in materials characterization. G. Havrilla and T. Miller; Powder Diffraction, June 2004, 19, 2, 119-126.

6. I have reviewed International Publication No. WO 90/15070 to Pirrung et al. and U.S. Patent No. 4,436,826 to Wang that have been cited by the U.S. Patent and Trademark Office as a basis for rejecting my invention as being obvious. I have compared the Pirrung and Wang references to my invention as disclosed and now claimed in the present patent application. After reviewing the Pirrung and Wang references, it is my firm conviction that these references do not render my invention obvious.

7. My invention is a method for detecting a binding event between members of a surface-bound receptor array and at least one potential binder using micro-x-ray fluorescence spectroscopy. My invention uses X-ray fluorescence as a probe to detect binding events between receptors and potential binders. In particular, my invention includes a method for detecting a binding event between at least one binder and members of a receptor array. The receptors are exposed to at least one binder and then arrayed on a substrate. The array is then exposed to X-ray radiation and an X-ray fluorescent signal from any bound member of the array is detected and used to determine where a binding event has occurred.

8. The combination of the Pirrung and Wang references does not yield my invention for at least three reasons:

- (i) First, Pirrung and Wang both require radioactive or fluorescent tags or labels to measure the sample whereas my invention uses no tagging whatsoever.
- (ii) In Wang, it is the fluorescent tag that is the source of the X-ray fluorescence signal. Without a tag, Wang would not be able to detect the XRF signal. In my invention, the XRF signal specifically comes from the bound member(s) of the array and not from a tag.
- (iii) Wang uses tags that are “unassociated chemically” with the component being analyzed. In order to be “unassociated chemically,” Wang encloses the tag in latex or a similar coating. In contrast, my invention measures elements that are chemically associated and that are intrinsically integral to the component bound and being measured.

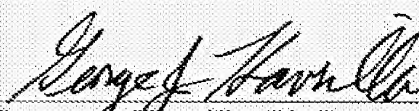
9. Accordingly, it is my opinion after reviewing the Pirrung and Wang references that these references do not render my invention obvious.

10. I declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful, false statements and the like are

punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and such willful, false statements may jeopardize the validity of any patents issued from the patent application.

Respectfully submitted,

Date: 10/18/2007


George J. Vavrilla, Ph.D.